REMARKS

Reconsideration and withdrawal of the rejections of the application respectfully requested in view of the remarks herewith, which place the application in condition for allowance.

I. Status Of Claims And Formal Matters

Claims 1-28, 31, 42-44, 57, and 58 are pending in this application. Claim 1 has been amended to recite a selection of cytokines in the cell growth medium. Support for this amendment can be found throughout the specification, for example page 21, lines 10-16, in Examples 1 and 3, in Table 1, page 38, and on page 34, lines 12-28.

No new matter has been added.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. §112. The amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

II. The Rejections Under 35 U.S.C. §112, Second Paragraph, Are Overcome

Claims 1-28, 31, 42-44, 57 and 58 are rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 1 recited in part (a) the limitation "cell growth medium comprising fetal bovine serum having a concentration of between 0% and 30% and methyl cellulose having a concentration of between 0.4% and about 0.7%, and transferrin and in an atmosphere having between about 3.5% oxygen and 7.5% oxygen. The Office Action alleges that there is insufficient antecedent basis for this particular combination of specific elements in a cell growth medium in the specification. Applicants respectfully disagree.

Applicants respectfully direct the Examiner to page 34, line 34 to page 35 line 24, which clearly recites the claimed limitation. Specifically, the serum-containing cultures of page 34 contains methyl cellulose at a final concentration of 0.7%, fetal bovine serum and transferrin (see e.g., page 34, lines 13-18). Furthermore, the samples are incubated in an atmosphere of 5% CO2 and 5% oxygen (see e.g., page 35, lines 19-24). Accordingly, there is sufficient antecedent support for this particular combination of specific elements in a cell growth medium in the

specification. Furthermore, this particular combination does flow from the specification as it is supported in the specification as originally filed and thus is not new matter.

Claim 1 has been clarified to recite in the medium at least one cytokine selected from the group consisting of erythropoietin, granulocyte-macrophage colony stimulating factor, granulocyte colony stimulating factor, macrophage colony stimulating factor, thrombopoietin, stem cell factor, interleukin-1, interleukin-2, interleukin-3, interleukin-6, interleukin-7, interleukin-15, Flt3L, leukemia inhibitory factor, insulin-like growth factor, and insulin.

This particular combination of specific elements in a cell growth medium is found throughout the specification thereby obviating the rejection. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, are respectfully requested.

II. The Rejections Under 35 U.S.C. §112, First Paragraph, Are Overcome

Claims 1-28, 31, 42-44, 57 and 58 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Office Action alleges that the specification does not appear to provide literal or adequate descriptive support for the recitation in part (a) of claim 1 of "cell growth medium comprising fetal bovine serum having a concentration of between 0% and 30% and methyl cellulose having a concentration of between about 0.4% and about 0.7% and transferring and in an atmosphere having between about 3.5% oxygen and 7.5% oxygen." The Office Action claims that nowhere in Applicant's disclosure appears to provide or teach such particular combination of the specific elements in a cell growth medium. Further, that none of the originally filed claims also recited the limitation in question and that the particular combination of elements in the culture growth medium as recited in claim 1 does not flow from the specification and is therefore considered to encompass new matter.

Claim 1 has been amended to recite in the medium at least one cytokine selected from the group consisting of erythropoietin, granulocyte-macrophage colony stimulating factor, granulocyte colony stimulating factor, macrophage colony stimulating factor, thrombopoietin, stem cell factor, interleukin-1, interleukin-2, interleukin-3, interleukin-6, interleukin-7, interleukin-15, Flt3L, leukemia inhibitory factor, insulin-like growth factor, and insulin.

This particular combination of specific elements in a cell growth medium is found throughout the specification thereby obviating the rejection. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, are respectfully requested.

III. The Rejections Under 35 U.S.C. §103 Are Overcome

Claims 1-28, 31, 42-44, 57 and 58 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Crouch et al. (Journal of Immunological Methods, 160:81-88 (1993)) in view of Bell et al. (US 2002/0120098 A1) and in further view of Moore et al. (U.S. Patent No. 5, 328, 844).

The Office Action alleges that it would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the culture growth media composition as taught by Bell having 30% fetal bovine serum, 0.8% methyl cellulose, and in an atmosphere having between about 5% oxygen, and to include therein transferrin taught by Moore, for the culture system as taught by Crouch for maintaining cells suitable for ATP bioluminescence assay, because Bell specifically taught that hematopoietic progenitor cells or stem cells favor survival and growth in a medium having such composition for use in any proliferation assays.

Further, the Examiner asserts that one of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the culture system as taught by Bell and complimented with transferrin by Moore, which stimulates proliferation of hematopoietic cells in culture growth media, for subsequent use as MNC sample for testing proliferation status using the ATP bioluminescence assay as taught by Crouch, because methyl cellulose is conventionally known to advantageously increase viscosity of proliferating cells in culture media, and transferrin as taught by Moore is conventionally known to advantageously provide iron protein transport for cells in the media, and Bell specifically taught that erythroid progenitor colony formation is even further enhanced at lower, more physiological oxygen tensions, i.e., 5% oxygen; hence, increasing the concentration of hematopoietic progenitor cells for use in assays that measure proliferation of cell populations, including the ATP bioluminescence assay taught by Crouch.

The Applicants respectfully disagree. It is respectfully submitted that it is well-settled that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further still, "obvious to try" is not the standard under 35 U.S.C. §103. *In re Fine,* 5 U.S.P.Q. 2d 1596, 1599 (Fed. Cir. 1988). And, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the

Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification." Also, the Examiner is respectfully reminded that for the Section 103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). Finally, the MPEP 2143.03 states in part that "To establish *prima facie* obviousness of a claimed invention, all claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)".

The present invention is directed to a high-throughput assay method for rapidly determining the proliferative status of isolated hematopoietic stem and progenitor cells and of subpopulations of differentiated cells thereof. Therefore, one of ordinary skill in the art at the time of the instant invention seeking to isolate and propagate hematopoietic stem and progenitor cells would not turn to Bell because Bell teaches away from the present invention. Bell involves preparation and use of growth media designed to stimulate hematopoietic progenitor growth, *specifically erythroid progenitors*. In fact, as the Abstract points out, the selection of components has an effect specific to erythropoiesis "as evidenced by a lack of growth of non-erythroid progenitors such as CFU-GM." (Last sentence, Abstract). Therefore, the cell growth medium of Bell is specifically designed not to induce any other kind of hematopoietic progenitor cells.

Furthermore, the Applicant specifically disagrees with the Examiner at page 6 of the Office Action, that "Bell et al. disclose compositions and methods comprising heme-containing components for use in inducing and/or enhancing stimulation of hematopoiesis (erythropoiesis)..." Hematopoiesis is the formation of blood cellular components, whereas erythropoiesis is the process by which erythrocytes are produced. These two terms do not describe the same thing. Therefore, whereas the present invention seeks to propagate any stem or progenitor cells of the hematopoietic system, Bell is only concerned with cells involved in erythropoiesis i.e., erythroblasts, erythrocytes.

Furthermore, it would not have been obvious to one skilled in the art at the time of the present invention to add the transferrin discussed in Moore. Moore is concerned with culture media that are formulated and optimized for the establishment and maintenance of effective mammalian cell growth in culture for either general or specialized purposes. The addition of transferrin to the growth media in Moore was believed to be for the general purpose of

transporting iron into cells (column 14, lines 38-46), but nowhere in Moore is it specifically taught to use transferrin to stimulate hematopoiesis. On the other hand, Moore does specifically address hematopoiesis with respect to other media supplements, for example 2-mercaptoethanol (column 8, lines 23-24), stating that "2-mercaptoethanol...has supported cell growth, especially of hematopoietic cells." As Moore itself point out, different cell types require different compositions of growth media - "Such media are distinguished from one another in that they contain critically different components in precise amounts." Therefore, whereas transferrin might have been recommended as a supplement to media for mammalian cells, it could not be known whether transferrin would have a beneficial effect on all cells of the hematopoietic system until the same had been attempted, which the present invention accomplishes.

Additionally, accompanying this response is a true copy Declaration under 37 C.F.R. §1.132 by Dr. Ivan N. Rich, who is the inventor of the present application. The statements in paragraph 6 of the Declaration provide further support that it would not have been obvious to one skilled in the art at the time of the present invention to add the transferrin discussed in Moore. Paragraphs 5 and 7 of the Declaration refute that "methyl cellulose is conventionally known to advantageously increase viscosity of proliferating cells in culture media", as is stated on page 8 of the Office Action.

Finally, as the Examiner correctly asserts, Crouch does not teach the cell growth culture medium disclosed in the present invention. Unlike Bell, Moore, or Crouch, the present invention discloses the addition to growth media of at least one cytokine selected from the group consisting of erythropoietin, granulocyte-macrophage colony stimulating factor, granulocyte colony stimulating factor, macrophage colony stimulating factor, thrombopoietin, stem cell factor, interleukin-1, interleukin-2, interleukin-3, interleukin-6, interleukin-7, interleukin-15, Flt3L, leukemia inhibitory factor, insulin-like growth factor, and insulin. Therefore, none of the references cited by the Examiner either alone or in combination provided the necessary incentive or motivation for modifying the reference teachings to arrive at the present invention.

Applicants remind the Examiner that it is impermissible to engage in a hindsight reconstruction of the claimed invention, using the Applicant's structure as a template, and selecting elements from references to fill in the gaps. *Interconnect Planning*, 744 F.2d 1132, 1143 (Fed. Cir. 1985). Applicants believe that only through the exercise of impermissible hindsight have the cited references been selected and relied upon by the Office. There is no

teaching or suggestion in the cited art to motivate one of ordinary skill in the art to combine elements of the references to result in the presently claimed invention.

For the above reasons, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103 are respectfully requested.

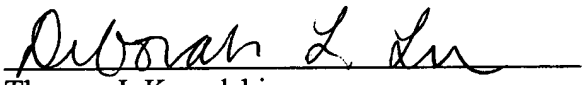
REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested; and, the Office Action is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the amendments, remarks and Declaration submitted herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: 

Thomas J. Kowalski
Reg. No. 32,147
Deborah L. Lu
Reg. No. 50,940
Telephone: (212) 588-0800
Facsimile: (212) 588-0500